The significant post-mortem findings were as follows. Slight icterus; throat merely slightly injected. A coiled embolus 1 cm. in diameter lay across the bifurcation of the pulmonary artery. The embolus was massive and as much as 25 cm. could be removed in one piece; the right side of the heart was acutely dilated. On dissection of the leg veins both femorals were found to be clear, but the intramuscular tributaries on the right side contained thrombus; it was concluded that embolus had originated in the right femoral vein. On the anterior wall of the rectum there was an elevated irregular area of ulceration 4 by 2 cm. which extended into the anal canal. The necrotic tissue was greenish on the surface and dull yellow underneath. The necrosis extended into the bowel wall for 3 cm. and the adjacent tissues were severely inflamed and oedematous. The bone marrow was hyperplastic, red marrow extending half-way down the femur. The spleen weighed 250 g., and neither it nor any of the other blood-forming tissues showed evidence of leukaemia. The liver showed merely toxic cloudy swelling.

On microscopical examination the rectal ulcer showed the typical appearance of an agranulocytic lesion, the cellular infiltrate being composed almost entirely of mononuclears, and necrosis and inflammatory oedema being very severe and widespread. The marrow contained numerous foci of erythroblasts, and megakaryocytes were also plentiful; polymorphs were absent and myelocytes were scanty. The marrow thus showed a severe maturation arrest of granulopoiesis amounting to aplasia, but no evidence of either leukaemia or panmyelophthisis.

COMMENT

The post-mortem findings establish the cause of death as pulmonary embolism following right femoral thrombosis in a case of agranulocytosis. The neutropenia was clearly due to failure of granulopoiesis without there being any disease process in the marrow to account for it. Since there was nothing to suggest splenic neutropenia (Hutchison and Alexander, 1954), and no history of cyclic attacks, but a clear history of the habitual use of novalgin, a sulphonated compound of amidopyrine known to have caused agranulocytosis, it seems reasonable again to incriminate this drug. The findings in our case correspond closely with previous accounts of agranulocytosis due to novalgin (Benjamin and Biederman, 1936; Klumpp, 1937; Plum, 1937); in particular, the unusually low white-cell count which we observed has been met with in other novalgin cases (Fitz-Hugh and Comroe, 1933; Ridpath, 1934), and ulceration of the rectum is recorded in the case described by Buck (1929).

The introduction of antibiotics has altogether transformed the prognosis in cases of agranulocytosis by controlling the generalized infections which formerly proved rapidly fatal. It seems probable that had embolism not occurred this patient's life might not have been forfeit to novalgin, for under treatment with penicillin she was not profoundly ill and her blood culture was negative. It is, however, evident from examination of her marrow after death that several more days would have been required to see her out of the danger period due to agranulocytosis; the precursors of the polymorphs had not returned to the marrow, and so recovery was not yet in sight.

We are grateful to Professor C. F. W. Illingworth for permission to report this case.

H. E. HUTCHISON, M.D.,
Senior Lecturer in Pathology, University of Glasgow.
HUGH CONWAY, M.B., B.Sc., M.R.C.P.,
Senior Registrar in Medicine, Western Infirmary, Glasgow.

REFERENCES

Benjamin, J. E., and Biederman, J. B. (1936). *J. Amer. med. Ass.*, **107**, 493.
Buck, R. W. (1929). Ibid., **93**, 1468.
Fitz-Hugh, T., and Comroe, B. I. (1933). *Amer. J. med. Sci.*, **185**, 552.
Hutchison, H. E., and Alexander, W. D. (1954). *Blood*, **9**, 986.
Klumpp, T. G. (1937). *J. Amer. med. Ass.*, **108**, 637.
Lancet, 1951, **1**, 389.
Plum, P. (1937). *Clinical and Experimental Investigations in Agranulocytosis*. Lewis, London.
Ridpath, R. F. (1934). *Arch. Otolaryng. (Chicago)*, **20**, 765.

Thomas's Sign, or the Silver Stool in Cancer of the Ampulla of Vater

Dr. A. M. Thomas, pathologist to the Royal Masonic Hospital, has pointed out that in cancer involving the ampulla of Vater the patient sometimes passes "silver stools"—that is, motions having the colour of oxidized silver or aluminium paint. The silver or grey stool is a combination of the white stool of obstructive jaundice and the black stool of melaena.

Biliary obstruction, whatever its cause, will produce a clay-coloured stool. Such a stool may contain blood from many sources. If the amount of blood is small it will not colour the stool appreciably. If it is large it will dominate the picture and lead to the typical black stool of melaena, but massive intestinal haemorrhage is either intermittent or fatal. If the blood comes from low down it will be red and not black. The combination of deep jaundice with steady intestinal haemorrhage coming from high up in the intestinal tract is seen regularly in cancer of the ampulla, and only rarely in other conditions.

CASE 1

A married woman aged 46 was admitted on September 30, 1952, with a history of intermittent jaundice for three months. She did not appear to have lost weight, but was very anaemic. Tests showed the jaundice to be of the obstructive type, and the stools contained occult blood in large amounts. The barium meal was reported to be normal, apart from spasticity of the pyloric antrum.

A laparotomy was performed on October 16. A carcinoma could be felt at the ampulla. The gall-bladder and common bile duct were grossly distended, and both contained white bile only. Cholecystostomy was performed. The discharge from the drain soon became green in colour. On October 30 pancreatico-duodenectomy was performed with ligature of the stump of the pancreas and implantation of the bile duct in the jejunum. Apart from some blood-stained discharge, convalescence was satisfactory.

Since discharge on January 1, 1953, the patient has remained very well, needing only small doses of insulin. She dislikes fats, but that has benefited two people—her in that she has regained her youthful figure, and me in that she sends me a regular supply of Devonshire cream.

CASE 2

A man aged 78 was admitted on February 14, 1954, with a suprapubic fistula, following prostatectomy at another hospital in November, 1953. His haemoglobin level was 50% and his general condition poor. He was given two pints (1,130 ml.) of packed cells, and shortly afterwards developed jaundice which at the time was attributed to the transfusion. His stools were sent for analysis, and Dr. Thomas reported that they had the silvery appearance that he had previously noted in Case 1. On this appearance he made a tentative diagnosis of carcinoma of the ampulla of Vater.

The jaundice deepened and the patient died on February 22 in hepatic failure. At necropsy a carcinoma 3 mm. in diameter was found at the ampulla of Vater. The haemorrhage on which the diagnosis had been made had, however, come from a colonic diverticulum.

COMMENT

The diagnosis has since been made in two further cases. So far as I am aware the silver stool has never been described before. I bring the sign to the attention of surgeons because Dr. Thomas has not yet reported it himself and, being a pathologist, he is likely to report it in a journal read only by his brother pathologists. Thomas's sign, which can be observed by a house-surgeon or nurse who is aware of its importance, is diagnostic of cancer of the ampulla of Vater, and will enable instances of this eminently curable lesion to be recognized at an early and operable stage.

HENEAGE OGILVIE, D.M., M.Ch.,
Consulting Surgeon,
Guy's Hospital and Royal Masonic Hospital.